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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/576,005	03/28/2006	Georg Szalkiel	195.66	9324

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EXAMINER	
WILDER, CYNTHIA B	

ART UNIT	PAPER NUMBER
1637	

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03/25/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/576,005	SCZAKIEL ET AL.	
	Examiner	Art Unit	
	CYNTHIA B. WILDER	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 January 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-14* is/are pending in the application.

4a) Of the above claim(s) *8-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-7 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed 1/15/2008 is acknowledged and has been entered. Claims 1-4 have been canceled. Claims 5-14 have been added and are pending in the instant invention. All of the arguments have been thoroughly reviewed and considered but are deemed moot in view of the new grounds of rejections necessitated by Applicant's amendment of the claims. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims.

This action is made FINAL.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Priority

3. Applicant's argument concerning priority benefit for the foreign document RU 2003125486 filed August 18, 2003 is acknowledged. However, Applicant is reminded to overcome an intervening prior art document, a certified copy of the priority document along with a translation of the document is required (see MPEP 1870). Since Applicant has not meet these conditions, the non-patent document of Rykova is considered valid prior art.

Election/Restrictions

4. Applicant's election of the Species Lung Cancer and the diagnostic markers APC and RASSF1A in the reply filed on 1/15/2008 is acknowledged. Because applicant did

not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). The claims which read on the elected species are claims 5-7 and 14. Accordingly, the claims 8-13 are withdrawn from consideration as being drawn to a non-elected invention.

Previous Rejections

5. The prior art rejections have been withdrawn in view of Applicant amendment cancelling the claims 1-4.

New grounds of Rejections

THE NEW GROUND(S) OF REJECTIONS WERE NECESSITATED BY APPLICANT'S AMENDMENT OF THE CLAIMS:

Claim Rejections - 35 USC § 102(a)

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

7. Claims 5 and 14 are rejected under 35 U.S.C. 102(a) as being anticipated by Rykova et al (citation made of record). With regards to claim 5, Rykova et al teach a method for the diagnosis of a disease, wherein the disease is breast cancer (abstract and page 218), the method comprising the steps of dividing the blood sample of the patient into plasma and cellular fractions, isolating extracellular from the plasma or

serum and determining by means of PCR, hybridization or sequencing whether at least two or more nucleic acids are presented among the isolated extracellular nucleic acids, the at least two nucleic acids (RASSF1A and HIC-1) being diagnostic markers indicative of a disease (page 218).

With regards to claim 14, Rykova et al teach the method according to claim 5, wherein the isolation of extracellular nucleic acids bonded to the surface of the cells of the cellular reaction is carried out by treating the cells with 10 volumes of PBS with 5 mmol/ 1 EDTA at 4 degrees Celsius; pelleting of the cells by centrifugation and collection of the supernatant; treating the cells with 0.25% trypsin solution; inactivation of trypsin with a trypsin inhibitor; pelleting of the cells by centrifugation and collection of the supernatant and isolation of extracellular nucleic acid from the collected supernatant with known methods (page 218).

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 5-6 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gocke et al (citation made of record in prior Office action) in view of Hefeneider et al (20020107372, August 8, 2002). With regards to claim 5-6, Gocke et al teach a method for the diagnosis of a disease, wherein the disease is lung cancer (see page 50, lines 25-30), the method comprising the steps of dividing the blood sample of the patient into plasma and cellular fractions, isolating extracellular from the plasma or serum and determining by means of PCR, multiplex amplification, hybridization or sequencing whether at least two or more nucleic acids are presented among the isolated extracellular nucleic acids, the at least two nucleic acids (APC, p53, and DCC) being diagnostic markers indicative of a disease (see pages 18-20, 23, 26-33, see also page 53, lines 20-30 which teaches detection of multiple different tumor markers). Gocke et al teaches several methods for the isolation of extracellular nucleic acid in plasma or serum, including centrifugation steps (see pages 17-20)

Gocke et al do not teach wherein the isolation of cell-surface bound extracellular nucleic acids comprises the use of PBS/EDTA and a trypsin treatment.

With regards to claim 14, Hefeneider et al provides a general teaching for isolating extracellular nucleic acids which are bonded to the surface of cells of a cellular fraction. Hefeneider et al teach that extracellular DNA are associates with human

diseases (0010), including those associated with the lung (0107). Hefeneider et al teach steps of isolating the cell-surface bound extracellular nucleic acid, said method comprising treating the cells with EDTA and PBS, then treating the cells with a trypsin solution (0112 and 0116), Hefeneider et al teach that the trypsin treatment permit cell surface-bound plasmid DNA to be distinguished from internalized plasmid DNA (0120).

Because both Gocke et al and Hefeneider et al teach methods of isolating extracellular DNA for subsequent analysis, such as by PCR, it would have been obvious to one of ordinary skill in the art to substitute one method for the other to achieve the predictable results of isolating extracellular nucleic acid, such as from the surface of cells of a cellular fraction. One of ordinary skill in the art would have been motivated to target extracellular DNA for the benefit of screening for diseases in an individual as suggested by both Gocke et al and Hefeneider et al.

11. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gocke et al in view of Hefeneider et al as previously applied above and further in view of Zochbauer-Muller (The Oncologist, vol. 7, pages 451-457, 2002), Regarding claim 7, Gocke et al in view of Hefeneider et al teach a method for diagnosing a disease as previously described above, wherein the disease is lung cancer and wherein one of the markers comprise APC.

Gocke et al in view of Hefeneider et al do not teach wherein the diagnostic marker indicative of lung cancer includes RASSF1A.

Zochbauer-Muller et al provides a general teaching of diagnostic markers that are associated with lung cancer. Zochbauer-Muller et al teach the diagnostic marker RASSF1A. Zochbauer-Muller et al teach that RASSF1a methylation may be of prognostic impact in lung cancer patients. Zochbauer-Muller et al teach that patients whose tumors were RASSF1A methylated had a shorter overall survival than patients whose tumors were not RASSF1A methylated (see page 454, col. 2).

Zochbauer-Muller also teaches the marker APC and teaches that low APC methylation is associated a significantly longer survival in lung cancer patients than for patients with high APC methylation status (page 454, col. 2).

Given the multiplex amplification method for detecting diagnostic markers as taught by Gocke et al in view of Hefneider et al, it would have been obvious to one of ordinary skill in the art at the time of the claimed invention that any combination of gene markers, including APC and RASSF1A, could be predictably detected with a reasonable expectation of success. One of ordinary skill in the art at the time of the claimed invention would have been motivated to target the lung cancer diagnostic markers APC and RASSF1A based on the teaching of Zochbauer-Muller et al that these markers have prognostic impact for lung cancer and thus benefit a patient in regards to treatment strategies.

Conclusion

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CYNTHIA B. WILDER whose telephone number is (571)272-0791. The examiner can normally be reached on a flexible schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/CBW/
/GARY BENZION/
Supervisory Patent Examiner, Art Unit 1637